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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/815,509	03/31/2004	Anthony E. Bolton	355908-3951	8220
38706	7590	03/20/2006	EXAMINER	
FOLEY & LARDNER LLP 1530 PAGE MILL ROAD PALO ALTO, CA 94304			ARNOLD, ERNST V	
			ART UNIT	PAPER NUMBER
			1616	
DATE MAILED: 03/20/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/815,509	<b>Applicant(s)</b> BOLTON ET AL.	
	<b>Examiner</b> Ernst V. Arnold	<b>Art Unit</b> 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.  
     4a) Of the above claim(s) 21 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 March 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/1/04</u> . | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

The Examiner acknowledges receipt of Applicant's response to the restriction requirement filed on 01/13/2006. Applicant elected without traverse Group I invention claim 20 linked by claims 1-19. Claims 21 and 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Accordingly claims 1-20 are presented for examination on the merits. Please note that claims 1-19 will be examined in so far as they read upon the elected subject matter: wherein the endothelin-related disorder is primary pulmonary hypertension.

### ***Drawings***

The drawings are objected to because the text is blurry and hard to read. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application

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must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 2002/0051766) in view of Sakai et al. (JACC 1996, 28(6), 1580-1588) and Cooke et al. (International Angiology 1997, 16(4), 250-254).

Smith et al. teach a method of treating congestive heart failure in a human patient comprising treating an aliquot of the patient's blood ex vivo with at least one stressor selected from the group consisting of a temperature above or below body temperature, an electromagnetic emission and an oxidative environment, followed by administering the aliquot of treated blood to the patient (Abstract and claims 1-24). Smith et al. teach that congestive heart failure may be secondary to other causes such as hypertension (Page 1, [0005]). The stressors may be applied individually or in any combination, simultaneously or sequentially (Page 3, [0028] and claims 23 and 24). The volume of the aliquot is up to 400 ml and most preferably 10 ml (Page 3, [0028]). The

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modified aliquot is re-introduced into the subject's body by any route suitable for vaccination, preferably selected from intra-arterial, intramuscular, intravenous, subcutaneous, and intraperitoneal injections as well as oral, nasal and rectal administration (Page 3, [0027]). The oxidizing agent contains medical grade oxygen and ozone gas and is introduced into the aliquot such that it does not give rise to excessive levels of cell damage (Page 3, [0033]). The gas stream has an ozone content of up to about 300  $\mu\text{g/ml}$  and more preferably 30  $\mu\text{g/ml}$  (Page 3, [0033]). The gas stream is supplied preferably up to about 0.33 liters/min and most preferably about  $0.24 \pm 0.024$  liters/min (Page 3, [0033]). The electromagnetic emission is applied with UV lamps primarily emitting UV-C band wavelengths (Page 3, [0034]). The temperature stressor is applied so that the temperature of all or part of the aliquot is in the range of from about  $-5\text{ }^{\circ}\text{C}$  to about  $55\text{ }^{\circ}\text{C}$ ; most preferably  $42.5 \pm 1\text{ }^{\circ}\text{C}$  and in other embodiments the aliquot is cooled below body temperature within the range of  $-5\text{ }^{\circ}\text{C}$  to about  $36.5\text{ }^{\circ}\text{C}$  (Page 3, [0030-0032]). The stressors can be applied within the time range of about 60 minutes more preferably about 3 or about 3.5 minutes (Page 3, [0035]).

Smith et al. do not expressly disclose a method of alleviating the symptoms of, or prophylaxis of, primary pulmonary hypertension.

Sakai et al. teach that congestive heart failure accompanies pulmonary hypertension (Abstract).

Cooke et al. teach that autologous blood treated with a combination of all three stressors (heat, ultraviolet light and ozone) can improve blood flow parameters in patients suffering from restricted blood flow to the extremities (Raynaud's syndrome)

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(Abstract and page 250 right column paragraphs 1 and 2). Raynauds's syndrome can be treated with vasodilator therapy (Page 251, Materials and methods, Patients).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the congestive heart failure method of Smith et al. in alleviating the symptoms of, or prophylaxis of, primary pulmonary hypertension and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because pulmonary hypertension and congestive heart failure are intimately related as taught by Sakai et al. and that the method of Cooke et al. can improve distribution and microcirculatory blood flow as well as decrease vascular resistance following treatment (Page 252, right column, Peripheral blood flow measurements). It is obvious to one of ordinary skill in the art to use a method that provides vasodilation in the treatment of a disorder that requires vasodilation such as primary pulmonary hypertension.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly disclosed or suggested by the combined teachings of the cited references.

***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

EVA



JOHN PAK  
PRIMARY EXAMINER  
GROUP 1601